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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/743,781	03/28/2001	Daniel Paris	12062.105014	7516

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EXAMINER	
ANDERSON, JAMES D	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/743,781	PARIS ET AL.	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3 and 22-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 23-30* is/are rejected.

7)☒ Claim(s) *22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/ are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3, and 22-30 are presented for examination

Continued Examination Under 37 CFR § 1.114

A request for continued examination under 37 CFR § 1.114, including the fee set forth in 37 CFR § 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR § 1.114, and the fee set forth in 37 CFR § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR § 1.114. Applicant's submission filed on 10/31/2007 has been entered.

Status of the Claims

Applicants' amendment filed 10/31/2007 has been received and entered into the application. Accordingly, claims 22 and 27-29 have been amended.

Applicants' arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Priority

In the previous Office Action, the Examiner indicated that no support was found in U.S. Provisional Application No. 60/092,570 for the specific administration of secretory phospholipase A2 inhibitors or for the treatment of cerebral amyloid angiopathy or vascular

amyloidosis. As such, the Examiner did not afford the instant claims the benefit of the filing date of the '570 application.

Applicants submit that at page 21 of the '570 application, administration of secretory phospholipase A2 inhibitors to block Aβ vasoactivity is disclosed. Upon further consideration, the Examiner is in agreement with Applicants that the '570 application provides support for the administration of a secretory phospholipase A2 inhibitor, specifically oleyloxyethylphosphocholine, to modify Aβ vasoactivity.

Applicants further submit that the '570 application teaches the ability to modulate the inflammatory and vasoactive effects of amyloid-beta, providing the basis for novel therapeutic intervention in diseases such as Alzheimer's (pages 3-4). Because cerebral amyloid angiopathy and vascular amyloidosis are known conditions associated with the vascular pathology of Alzheimer's disease, Applicants assert that a method of treating the vascular aspects of Alzheimer's would inherently treat such associated vascular conditions as cerebral amyloid angiopathy and vascular amyloidosis. However, the Examiner respectfully submits that the instant claims recite the treatment of "other vascular-related diseases or disorders" (*e.g.*, cerebral amyloid angiopathy and vascular amyloidosis). As such, there is no requirement in the instant claims that the patient being treated has Alzheimer's disease. The fact remains that the '570 application does not disclose the treatment of cerebral amyloid angiopathy or vascular amyloidosis. Accordingly, the Examiner is not persuaded that the '570 application provides support the claimed limitation of treating cerebral amyloid angiopathy or vascular amyloidosis with a phospholipase A2 inhibitor.

Because any given claim can only have one priority date and all claims depend from claim 1 which recites the treatment of cerebral amyloid angiopathy and vascular amyloidosis, the instant claims are not afforded the priority date of the '570 application. The earliest effective U.S. filing date afforded the instant claims is **7/13/1999**, the filing date of PCT/US99/15947 of which the instant application is a 371.

Claim Rejections - 35 USC § 112 (1st Paragraph)

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, and 23-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modifying beta-amyloid-induced vasoactivity in individuals with Alzheimer's disease or other vascular-related diseases or disorders comprising administering oleyloxyethylphosphocholine, does not reasonably provide enablement for modifying beta-amyloid-induced vasoactivity in individuals with Alzheimer's disease or other vascular-related diseases or disorders comprising administering any and all sPLA2 inhibitors as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. This is a Scope of Enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.

In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence or absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA

[1] As pointed out by the court in *In re Angstadt*, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the *Wands* factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill of those in the art

The invention relates to a method of modifying beta-amyloid-induced vasoactivity in individuals with Alzheimer's disease or other vascular-related diseases or disorders selected from the group consisting of cerebral amyloid angiopathy, vascular amyloidosis, hypertension, and vasospasm associated with severe post-traumatic head injury comprising administering an inhibitor of sPLA2.

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. The artisan using Applicant's invention would generally be a physician with a M.D. degree and several years of experience.

That factor is outweighed, however, by the unpredictable nature of the art. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte Sudilovsky* 21 USPQ2d 1702 (Appellant's invention

concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain).

In the instant case, there is no evidence of record that sPLA2 inhibitors as broadly encompassed by the claims could predictably be used to treat the broad scope of the claimed diseases and disorders. In fact, only one sPLA2 inhibitor has been shown to inhibit of Aβ vasoactivity *in vitro*.

2. The breadth of the claims

The claims vary in breadth; some (such as claim 1) vary broadly, reciting a method of modifying beta-amyloid-induced vasoactivity in individuals with Alzheimer's disease or other vascular-related diseases or disorders selected from the group consisting of cerebral amyloid angiopathy, vascular amyloidosis, hypertension, and vasospasm associated with severe post-traumatic head injury comprising administering an inhibitor of sPLA2. Others, such as claims 25 and 26, are narrower, reciting specific vascular-related diseases or disorders (claims 25 and 26). All, however, are extremely broad insofar as they disclose the general treatment of vascular-related diseases or disorders with the same sPLA2 inhibitors.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for determining the particular administration regimens (*e.g.*, dosages, timing, administration routes, etc.) necessary to treat all of the various diseases or disorders claimed, particularly in humans. The direction concerning treating the claimed diseases and disorders is found in the specification at pages 15-37, which provide cellular and *in vivo* assays demonstrating that Aβ mediates its vasoactive effect by activating specific PLA2 isoforms and that a single sPLA2 inhibitor (oleyloxyethylphosphocholine) blocks Aβ vasoactivity. However, no models of the claimed diseases are described, so Applicants have provided no specific guidance with respect to the treatment of these conditions. Applicants describe formulations at pages 12-15. Doses required to practice their invention are described at page 15. A 10^6-fold range of doses is recommended (*e.g.*, 100 ng/kg to 100 mg/kg body weight/day). The claims encompass 0.1 ng to 10 mg/kg body weight/day. Since only one sPLA2 as instantly claimed has been used to inhibit Aβ induced vasoactivity *in vitro*, how is the skilled physician to know what dose to use for each of these pathologically different conditions and structurally diverse compounds encompassed by "sPLA2 inhibitor"? There are no guidelines for determining the doses needed to treat hypertension *vs.* cerebral amyloid angiopathy *vs.* vasospasm associated with severe post-traumatic head injury. Are the identical doses to be used for treating these unrelated conditions? There are *in vitro* assays demonstrating that Aβ mediates its vasoactive effect by activating specific PLA2 isoforms and that a single sPLA2 inhibitor (oleyloxyethylphosphocholine) blocks Aβ vasoactivity. However, it is unclear if these assays correlate to the treatment of all of the

diseases encompassed by the claims or if the activity of oleyloxyethylphosphocholine correlates to the activity of all sPLA2 inhibitors. Further, inhibition of a receptor *in vitro* does not predictably correlate to clinical efficacy. As such, it is not predictable that simply because a compound inhibits sPLA2 *in vitro* it will also be effective in treating beta-amyloid-induced vasoactivity in patients having the claimed diseases and disorders.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art (as discussed *supra*) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that the instantly claimed genus of compounds, defined only by biological activity (*i.e.*, inhibition of sPLA2) could be predictably used to modify beta-amyloid-induced vasoactivity in patients having any of the claimed diseases and disorders as inferred in the claims and contemplated by the specification.

Genentech Inc. vs. Nova Nordisk states, "[A] patent is not a hunting license. It is not a reward for a search but a compensation for its successful conclusion and 'patent protection' is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" (42 USPQ 2d 1001, Fed. Circuit 1997).

In the instant case, Applicants have presented a general idea that because the sPLA2 inhibitor oleyloxyethylphosphocholine blocks Aβ vasoactivity *in vitro*, then it and all sPLA2 inhibitors must therefore, *a priori*, be useful in the treatment of beta-amyloid-induced vasoactivity in patients having anyone of five different diseases or disorders as recited in claim 1. However, the claims encompass an unknown number of sPLA2 inhibitors (perhaps thousands)

having a plethora of chemically and biologically distinct substituents. Applicants tested one such sPLA2 inhibitor for inhibition of Aβ vasoactivity *in vitro*.

Determining if any particular claimed compound would treat any particular disease state would require identification of an agent that inhibits sPLA2, formulation into a suitable dosage form, and subjecting it to clinical trials or to testing in an assay known to correlate to clinical efficacy of such treatment. This is undue experimentation given the limited guidance and direction provided by Applicants. As noted *supra*, even *in vitro* and *in vivo* assays do not always correlate to efficacy in humans and are not generally predictive of clinical efficacy.

Accordingly, the instant claims do not comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The instant claims recited methods of modifying beta-amyloid-induced vasoactivity in individuals with Alzheimer's disease or other vascular-related diseases or disorders comprising

administering a secretory phospholipase A2 (sPLA2) inhibitor in an amount ranging from 0.1 ng to 10 mg/kg body weight/day (*e.g.*, claim 1).

Claims 1, 3, 23, 24, and 27-30 rejected under 35 U.S.C. 102(b) as being anticipated by **Watanabe** (WO 99/25340; Published May 27, 1999) (newly cited).[2]

Watanabe teaches a method for the prevention and treatment of Alzheimer's disease by administering to a human in need thereof an effective amount of a substituted tricyclic sPLA2 inhibitor (Abstract; page 2, lines 29-35).

With respect to the doses recited in instant claim 1, Watanabe teaches that for oral dosing, one to four oral doses per day, each from 0.01 to 25 mg/kg are administered (page 78, lines 15-17).

With respect to the administration routes recited in claims 27-28, Watanabe teaches that the disclosed sPLA2 inhibitors can be administered orally (page 78, lines 15-17), parenterally (page 78, lines 18-28), or *via* inhalation (page 78, lines 29-32), thus meeting the limitations of claims 27 and 28.

With respect to the formulations recited in claim 29, Watanabe teaches such formulations, including solid dosage forms (*e.g.*, capsules, tablets, and powders) (page 74, lines 25-26) and liquids (*e.g.*, elixirs, syrups, or suspensions) (page 74, lines 27-28), thus meeting the limitations of claim 29.

With respect to claims 23, 24, and 30, which recite the treatment of cerebral amyloid angiopathy (claims 23 and 30) and vascular amyloidosis (claims 24 and 30), the Examiner refers to Applicants' response filed 10/31/2007 wherein they admit, citing Ellis *et al.* and Selkoe *et al.*,

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[2] As noted *supra*, the instant claims are afforded a priority date of 7/13/1999.

that cerebral amyloid angiopathy and vascular amyloidosis "are known conditions associated with the vascular pathology of Alzheimer's disease". As such, Applicants admit that a method for treating the vascular aspects of Alzheimer's disease would "inherently treat such associated vascular conditions as cerebral amyloid angiopathy and vascular amyloidosis" (see page 4 of Response file 10/31/2007). Accordingly, the treatment of Alzheimer's disease by administering the sPLA2 inhibitors as taught in Watanabe will necessarily result in the treatment of cerebral amyloid angiopathy and vascular amyloidosis as recited in claims 23, 24, and 30.

Watanabe is silent with respect to the instantly recited mechanisms of the claimed sPLA2 inhibitors (*e.g.*, modifying beta-amyloid-induced vasoactivity or down-regulating a soluble Aβ pro-inflammatory pathway) as recited in claims 1 and 3. However, practice of the methods of treating Alzheimer's disease as taught in Watanabe will inherently result in the claimed modification of beta-amyloid-induced vasoactivity or down-regulation of a soluble Aβ pro-inflammatory pathway. It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he

fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

Though Watanabe does not expressly teach modifying beta-amyloid-induced vasoactivity (claim 1) or down-regulating a soluble Aβ pro-inflammatory pathway (claim 3) as a result of the administration of the disclosed sPLA2 inhibitors to a patient having Alzheimer's disease, the administration of the same compound(s) as claimed (*e.g.*, those identical to Applicant's broadly claimed sPLA2 inhibitors) to the same host (*i.e.*, a patient having Alzheimer's disease) as claimed is considered to necessarily have the claimed effects of modifying beta-amyloid-induced vasoactivity or down-regulating a soluble Aβ pro-inflammatory pathway, on the subject being treated, whether expressly recognized by Watanabe or not. Products of identical chemical composition cannot exert mutually exclusive properties when administered under the same circumstances or, in the present case, the same host. Please reference MPEP §2112.

The explanation of an effect obtained when using a compound cannot confer novelty on a known process if the skilled artisan was already aware of the occurrence of the desired therapeutic effect. In other words, even if the modification of beta-amyloid-induced vasoactivity or down-regulation of a soluble Aβ pro-inflammatory pathway was not itself recognized as a pharmacological effect of administering the disclosed compounds of Watanabe for the disclosed therapeutic purpose(s) discussed therein, such an effect is not considered a new therapeutic application because a known therapeutic effect and benefit of using this same active compound(s) was already known in the prior art. Though mechanisms of action of chemical entities are not doubt important contributions to scientific and pharmaceutical development, the

assessment of patentability under 35 U.S.C. § 102 is based upon the therapeutic applications and therapeutic effects of the compounds, not the mechanism by which they exert such a therapeutic effect. Furthermore, it is generally well settled in the courts that a mechanistic property of a chemical compound, or combination of chemical compounds, when administered under identical conditions, is necessarily present, despite the fact that such a property may not have been readily apparent to, or recognized by, one of ordinary skill in the art.

Accordingly, claims 1, 3, 23, 24, and 27-30 are deemed properly rejected as being anticipated by Watanabe.

Claims 1, 3, 23, 24, and 27-30 are rejected under 35 U.S.C. § 102(e)(2) as being anticipated by **Watanabe** (USP No. 6,436,983 B1; Issued Aug. 20, 2002; Filed Nov. 14, 1998) (newly cited).

Watanabe teaches a method of treating a mammal, including a human, susceptible to or having Alzheimer's disease, comprising administering an effective amount of a 1H-indole-3-glycoxyamide sPLA2 inhibitor (Abstract; col. 1, lines 57-63).

With respect to the doses recited in instant claim 1, Watanabe teaches that for oral dosing, one to four oral doses per day, each from 0.01 to 25 mg/kg are administered (col. 17, lines 40-42).

With respect to the administration routes recited in claims 27-28, Watanabe teaches that the disclosed sPLA2 inhibitors can be administered orally (col. 17, lines 40-42), parenterally (col. 17, lines 43-53), or *via* inhalation (col. 17, lines 54-57), thus meeting the limitations of claims 27 and 28.

With respect to the formulations recited in claim 29, Watanabe teaches such formulations, including solid dosage forms (*e.g.*, capsules, tablets, and powders) (col. 15, lines 44-45) and liquids (*e.g.*, elixirs, syrups, or suspensions) (col. 15, lines 46-48), thus meeting the limitations of claim 29.

With respect to claims 23, 24, and 30, which recite the treatment of cerebral amyloid angiopathy (claims 23 and 30) and vascular amyloidosis (claims 24 and 30), the Examiner refers to Applicants' response filed 10/31/2007 wherein they admit, citing Ellis *et al.* and Selkoe *et al.*, that cerebral amyloid angiopathy and vascular amyloidosis "are known conditions associated with the vascular pathology of Alzheimer's disease". As such, Applicants admit that a method for treating the vascular aspects of Alzheimer's disease would "inherently treat such associated vascular conditions as cerebral amyloid angiopathy and vascular amyloidosis" (see page 4 of Response file 10/31/2007). Accordingly, the treatment of Alzheimer's disease by administering the sPLA2 inhibitors as taught in Watanabe will necessarily result in the treatment of cerebral amyloid angiopathy and vascular amyloidosis as recited in claims 23, 24, and 30.

Watanabe is silent with respect to the instantly recited mechanisms of the claimed sPLA2 inhibitors (*e.g.*, modifying beta-amyloid-induced vasoactivity or down-regulating a soluble Aβ pro-inflammatory pathway) as recited in claims 1 and 3. However, practice of the methods of treating Alzheimer's disease as taught in Watanabe will inherently result in the claimed modification of beta-amyloid-induced vasoactivity or down-regulation of a soluble Aβ pro-inflammatory pathway. It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a

product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

Though Watanabe does not expressly teach modifying beta-amyloid-induced vasoactivity (claim 1) or down-regulating a soluble Aβ pro-inflammatory pathway (claim 3) as a result of the administration of the disclosed sPLA2 inhibitors to a patient having Alzheimer's disease, the administration of the same compound(s) as claimed (*e.g.*, those identical to Applicant's broadly claimed sPLA2 inhibitors) to the same host (*i.e.*, a patient having Alzheimer's disease) as claimed is considered to necessarily have the claimed effects of modifying beta-amyloid-induced vasoactivity or down-regulating a soluble Aβ pro-inflammatory pathway, on the subject being treated, whether expressly recognized by Watanabe or not. Products of identical chemical composition cannot exert mutually exclusive properties when administered under the same circumstances or, in the present case, the same host. Please reference MPEP §2112.

The explanation of an effect obtained when using a compound cannot confer novelty on a known process if the skilled artisan was already aware of the occurrence of the desired

therapeutic effect. In other words, even if the modification of beta-amyloid-induced vasoactivity or down-regulation of a soluble Aβ pro-inflammatory pathway was not itself recognized as a pharmacological effect of administering the disclosed compounds of Watanabe for the disclosed therapeutic purpose(s) discussed therein, such an effect is not considered a new therapeutic application because a known therapeutic effect and benefit of using this same active compound(s) was already known in the prior art. Though mechanisms of action of chemical entities are not doubt important contributions to scientific and pharmaceutical development, the assessment of patentability under 35 U.S.C. § 102 is based upon the therapeutic applications and therapeutic effects of the compounds, not the mechanism by which they exert such a therapeutic effect. Furthermore, it is generally well settled in the courts that a mechanistic property of a chemical compound, or combination of chemical compounds, when administered under identical conditions, is necessarily present, despite the fact that such a property may not have been readily apparent to, or recognized by, one of ordinary skill in the art.

Accordingly, claims 1, 3, 23, 24, and 27-30 are deemed properly rejected as being anticipated by Watanabe.

Allowable Subject Matter

Claim 22 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson
Patent Examiner
AU 1614

January 25, 2008

Ardin H Marschel 1/27/08
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER